

REMARKS**I. Status of claims**

Claims 37, 42, 44, and 51 are pending. Claims 37, 42, 44, and 51 are rejected under 35 U.S.C. §103(a). Claim 37 is amended to more clearly recite the subject matter which Applicant regards as the invention. The amendment includes no new matter.

II. The rejection of claims 37, 42, 44, and 51 under 35 U.S.C. § 103(a) may be withdrawn.

Claims 37, 42, 44 and 51 are rejected under 35 U.S.C. § 103(a) as assertedly unpatentable over Lee *et al.* ("Lee") in view of Harlow and Lane ("Harlow and Lane"). Specifically, the Examiner asserted that Lee discloses a fragment comprising residues 251-264 of human tau. The Examiner further asserted that since the aforementioned fragment originated from brains of patients with AD, it comprises both phosphorylated and non-phosphorylated Serine at position 262, absent evidence to the contrary. Applicants respectfully traverse.

At the outset, Applicants point out that claim 37 has been amended to recite "tau" in subpart (a). It should also be noted that the present invention provides compositions and methods useful for the production of antibodies that differentiate between tau protein that is phosphorylated at Serine 262 versus tau protein that is not. The pending claims are drawn to a fragment of full length tau protein which makes up an epitope the Applicants have found significant in diagnosis of Alzheimer's disease. In this condition, serine amino acids at position 262 in tau proteins are hyper-phosphorylated, and an antibody produced using this epitope which can distinguish between the phosphorylated/dephosphorylated state of this residue in tau protein samples from a patient would be extremely helpful in diagnosing the patient's condition.

With respect to Lee, several paragraphs distinguish between A68 and tau (indeed the purpose of the Lee publication appears to be focused on determining the relationship between A68 and tau). For example, column 1 of page 676 states "Despite immunological and biochemical data that imply A68 is a modified form of τ , this hypothesis is controversial, and the mechanism whereby this modification could occur is unknown." Lee further notes that A68 has a higher M_r , a more acidic isoelectric point, and far lower

solubility in nonionic detergents than τ (column 2 of page 676). Nevertheless, even if tau is "derived" from A68 or vice versa, the fact that Lee disclose a fragment of A68 corresponding to amino acids 251-264 of tau does not mean it is similarly phosphorylated as tau.

Finally, Lee does not disclose or even suggest the specific phosphorylatable fragment/epitope of tau as set forth in the present claims, let alone such a fragment for the purpose of generating an antibody that can distinguish between phosphorylated and dephosphorylated tau. Furthermore, nowhere in Lee is the significance of the serine residue at position 262 disclosed as being significant in diagnosis of Alzheimer's disease as set out in the instant specification. As described above, this has been described for the first time by the present invention.

In view of the arguments set forth above, the Applicants submit the rejection of claims 37, 42, 44, and 51 under 35 U.S.C. § 103(a), may properly be withdrawn.

CONCLUSION

In view of the above arguments and amendments, Applicants believe the pending application is in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: June 19, 2007

Respectfully submitted,

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